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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,808	ETCHES ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3-11-08 has been entered.

Claims 1-9, 19 and 20 have been canceled. Claims 10-18 remain pending and under consideration.

Applicant's arguments filed 3-11-08 have been fully considered but they are not persuasive. Please separate arguments for each rejection with a heading. Arguments may be repeated or referred to under each heading; however, all arguments for each rejection must at least be referred to under each heading.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The amendment to the specification filed 3-11-08 has been entered and is correct. The sequence listing filed 3-11-08 has been entered and is correct.

Indefiniteness

Claims 10-18 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 as amended remains indefinite because the phrase “wherein a population of B lymphocytes produced by the chicken are comprised of an assembly of human immunoglobulin locus genes that undergo functional immunoglobulin gene conversion to encode a human immunoglobulin heavy or light chain immunoglobulin molecule” remains unclear. A B-cell can comprise a human gene but cannot comprise a human locus as claimed. B-lymphocytes do not “comprise” a “locus” i.e. a chromosome position. The position of the gene, i.e. the locus, does not describe the structure or function of the B-lymphocytes. The phrase “locus genes” does not clarify the claim because the phrase does not make sense and does not have a meaning in the art or the specification. Applicants argue the term locus was removed from the claim. Applicants’ argument is not persuasive. The term locus remains in the claim.

The metes and bounds of “conversion” in claim 10 are unclear. It cannot be determined if the claim requires “conversion" in the chimeric chicken or if the claim encompasses a human Ig gene that has already been “converted.” It is also unclear if “switching” and “rearrangement” are both encompassed by the term “conversion."

The phrase “pseudo” in claims 15 and 18 remains indefinite. It cannot be determined how “like” a human heavy chain V region a gene must be to be a “pseudo V gene” for example. Applicants argue the phrase is consistent with the phrase used in Eur. J. Immunol., 1993, Vol. 23, No. 10, pg 2448-2453, Benatar, Mol. Cell Biol., 1993,

Vol. 13, NO. 2, pg 821-830 and McCormack, Jan. 1995, Mol. Biol. Evol, Vol. 12, No. 1, pg 94-102. Applicants' argument is not persuasive because the references have not been provided. Furthermore, the references may use the phrase "pseudo"; however, applicants have not indicated the references define the metes and bounds of "pseudo" genes. Accordingly, those of ordinary skill would not know when an Ig gene had crossed the line and become "like" a human Ig gene.

Claim 16 remains indefinite because it is unclear how "switching" further limits "conversion" in claim 10, and the structure of the resulting IgG molecule after switching cannot be determined. In addition, it cannot be determine what applicants consider "class switching." The distinction between rearrangement and switching cannot be determined. Ultimately, the structure of the "isotype G immunoglobulin molecules" in the B-cells cannot be determined. Applicants argue the phrase is consistent with the phrase used in US patent 5,874,299 and 6,139,835. Applicants' argument is unfounded. The phrase is not defined in US patent 5,874,299 and 6,139,835 so that the structure of the isotype G immunoglobulin molecules in the B-cells can be determined. Applicants argue there is a difference between class switching and rearrangement (pg 11 of the response filed 3-11-08). The difference is not readily apparent and the structure of a gene after "switching" is not defined in Buelow (US Patent 7129084).

Claim Rejections - 35 USC § 102

Claims 10-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Rapp (Patent Application Publication US 2002/0108132 A1) for reasons of record.

Rapp taught a chimeric chicken whose genome comprised a transgene encoding a human heavy and/or light chain antibody comprising the V, D, C and J regions (paragraphs 63, 76, 151, 154, 161, 163).

Claims 10 and 16 are included because the B cells of the chicken inherently undergo immunoglobulin gene "conversion" or rearrangement class "switching" and yield isotype G immunoglobulin molecules. Without evidence to the contrary, the transgene taught by Rapp is capable of undergoing conversion or switching as claimed because the transgene of Rapp inherently encoded a switch region along with the human Ig heavy and light chains. In particular, the structure of the transgenic chicken in claim 16 is not distinguished over the structure of the transgenic chicken described by Rapp.

The phrase "wherein a population of B lymphocytes produced by the chicken comprise an assembly of human immunoglobulin locus genes that undergo functional immunoglobulin gene conversion to encode a human immunoglobulin heavy or light chain immunoglobulin molecule" in claim 10 is also included in part because the phrase "immunoglobulin locus genes" does not make sense; B lymphocytes cannot comprise a locus as claimed. The transgene taught by Rapp is equivalent to the transgene claimed because it comprises human Ig heavy and light chains and inherently comprises switch regions making it inherently capable of undergoing conversion or switching as claimed.

If claim 10 is intended to limit the transgenic chicken to a knock-in transgenic chicken, Rapp described making a knock-in transgenic chicken in paragraphs 80 and 121.

Claims 12-15 and 18 are included because the transgene may comprise a plurality of heavy or light chain V or D regions (paragraph 154). Claims 15 and 18 are included because the human immunoglobulin transgene is "like" the chicken immunoglobulin gene, i.e. "pseudo". The instant application does not define pseudo genes, thus leaving the meaning open to any reasonable interpretation.

Claim 17 is included because the antibody was expressed in the yolk of an egg produced by the chicken (paragraph 108).

Claim 18 is included because Rapp used the CMV promoter to express the transgene, which inherently expressed the transgene in all tissues, specifically in B-lymphocytes as claimed. The structure of the "B lymphocyte specific regulatory region" in claim 18 is not distinguished by structure or function over the CMV promoter described by Rapp.

Applicants argue Rapp did not teach the genes undergo functional Ig rearrangement. Applicants' argument is not persuasive. The B cells of the chicken described by Rapp inherently undergo immunoglobulin gene "conversion" or rearrangement class "switching" because the transgene of Rapp inherently encoded a switch region along with the human Ig heavy and light chains. In particular, the structure of the transgenic chicken in claim 16 is not distinguished over the structure of the transgenic chicken described by Rapp. Furthermore, the claims require "conversion" not "rearrangement."

Claims 10-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Buelow (US Patent 7129084) for reasons of record.

Buelow taught a vector encoding human variable, joining and diversity immunoglobulin genes capable of replacing endogenous immunoglobulin variable, joining and diversity regions. Specifically Buelow taught a BAC vector with a chicken light chain modified by homologous recombination (Fig. 13-15). The vectors are used to make knock-in chickens expressing human variable and joining regions of an immunoglobulin gene (Examples 12-14). The vectors inherently comprise B cell specific regulatory regions operably linked to the human immunoglobulin gene (claim 19) because they are linked to the endogenous chicken heavy chain gene (col. 26, Example 11). Chimeric chickens were obtained (col. 27, line 44). Without evidence to the contrary, the human Ig genes inherently undergo "conversion" or "switching" as claimed because they comprise switch regions.

Applicants argue the reference is not enabling. Applicants argue the data in Buelow is fictitious. Applicants argue transgenic chickens have never been made from ES cells. Applicants' argument is not persuasive. Each patent is presumed to be enabled unless proven otherwise. Applicants have not set forth why the teachings relied up on are not enabling. Applicants have not provided adequate evidence that the data is fictitious. Furthermore, the rejected claims do not require the transgenic chickens are made from ES cells and the teachings of Buelow are not limited to making transgenic chickens using ES cells. The structure of the transgenics taught by Buelow are the same as those now claimed. The teachings in Buelow are enabling because they are no less than those described by applicants in the instant application.

Claims 10-18 remain rejected under 35 U.S.C. 102(e) as being anticipated by Singh (US Patent Application Publication 2002/0028488) for reasons of record.

Singh taught a vector encoding human variable, joining and diversity immunoglobulin genes capable of replacing endogenous immunoglobulin variable, joining and diversity regions. Specifically Singh taught a vector with a chicken light and heavy chain modified by homologous recombination (Fig. 2-4). The vectors are used to make knock-in chickens expressing human variable and joining regions of an immunoglobulin gene. The vectors inherently comprise B cell specific regulatory regions operably linked to the human immunoglobulin gene (claim 19) because they are linked to the endogenous chicken heavy or light chain gene (pg 8, paragraph 84). Without evidence to the contrary, the human Ig genes inherently undergo "conversion" or "switching" as claimed because they comprise switch regions.

Applicants' argue Singh did not enable the claimed invention. Applicants argue the Singh publication is a farce. Applicants' argument is unfounded. Singh taught the method steps required to obtain the chimeric chicken claimed. It is unclear why applicants believe the reference is not enabled. It is unclear what specific method steps are lacking from Singh or why those of skill would not be able to apply the teachings of Singh to the chicken genome.

Applicants argue transgenic chickens were not available until US Patent 7,145,057. Applicants' argument is not persuasive. As stated in the first office action:

"Stage XI PGCs had been isolated from chickens, transduced with retrovirus, and immediately injected into the vasculature of Stage 15 chick embryos to obtain germline transmission of a transgene (Vick, Proc. R. Soc. Lond., 1993, Vol. 251, pg 179-182). Plasmid DNA had been injected into the germinal disc of chick zygotes isolated before being laid to obtain germline transmission

of a transgene (Love, Bio/Technology, 1994, Vol. 12, pg 60-63). Retroviral vectors had been injected into the subgerminal cavity of an avian embryo in a freshly laid egg to obtain germline transmission of a transgene (Thoroval, Transgenic Research, 1995, Vol. 4, pg 369-376). Retroviral vectors had been used to introduce a truncated antibody receptor into chickens "somatically" and express the receptor in the bursa at hatch (Sayegh, Dec. 15, 1999, Vol. 72, pg 31-37; pg 32, 2nd full para., lines 2-5 and 16-18; para. bridging pg 33-34)." Pg 5 of office action sent 1-11-07.

Double Patenting

Claims 10-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 11/062325 for reasons of record. Claim 8-11 of '325 are drawn to a genetically modified chicken expressing in tubular gland cells monoclonal antibodies encoded by an exogenous polynucleotide, wherein the monoclonal antibodies are present in egg white at a concentration of at least 40 .mu.g/ml. The product claimed in '325 is an obvious variant of the product claimed in the instant application and is described in the instant disclosure. The product claimed in this application is obvious in view of the claims of '089 taken with the disclosure of '089. This is a provisional obviousness-type double patenting rejection.

Claims 10-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/524089 for reasons of record. Claim 1-8 of '089 are drawn to A chicken selectively expressing exogenous protein in tubular gland cells wherein the protein is encoded by a transgene stably integrated into a genome of the chicken and wherein the transgene is comprised at least a portion of a promoter of a gene encoding an egg white protein that is operably linked to DNA encoding the exogenous protein.

The product claimed in '089 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '089. The product claimed in this application is obvious in view of the claims of '089 taken with the disclosure of '089. This is a provisional obviousness-type double patenting rejection.

Claims 10-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9-10 of copending Application No. 10/216098, now US Patent 7,323,618 for reasons of record. Claim 9-10 of '098 are drawn to a chimeric chicken selectively expressing exogenous protein in tubular gland cells, wherein the exogenous protein is encoded by a transgene stably integrated into a genome of a donor embryonic stem cell whose progeny contribute to the chimeric chicken, and wherein the transgene is greater than 15 kb in size and is comprised of an at least a 7.5 kb portion of an ovalbumin promoter operably linked to DNA encoding the exogenous protein. The product claimed in '098 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '098. The product claimed in this application is obvious in view of the claims of '098 taken with the disclosure of '098. This is a provisional obviousness-type double patenting rejection.

Claims 10-18 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7 and 9 of US Patent 6,861,572 for reasons of record. Claim 1, 7 and 9 of '572 are drawn to an egg-laying chicken whose somatic cells contain an expression system comprising (i) a first DNA sequence encoding a human gamma isotype immunoglobulin constant region having a CH2-CH3 region in an Fc domain of the constant region; (ii) a second DNA

sequence encoding a human immunoglobulin variable region; (iii) a third DNA sequence comprising an immunoglobulin-gene derived promoter sufficient for expression of the human immunoglobulin constant region in the chicken; wherein the egg-laying chicken produces eggs whose yolk contains human gamma isotype immunoglobulin having a constant region encoded by the first DNA sequence and a variable region encoded by the second DNA sequence. The product claimed in '572 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '572. The product claimed in this application is obvious in view of the claims of '572 taken with the disclosure of '572.

Claim 12 remains objected to under 37 CFR 1.75 as being a substantial duplicate of claim 14. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Applicants have not responded to any of the double patenting rejections.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner